UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

SEP 5 1989

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP# 7E 3489 CGA-154281 On All Crops with Tolerances for Metolachlor (Dual®). Evaluation of the July 7 and August 21, 1989 Amendments. (MRID No. 41208-02 and 411774-01) [DEB No. 5602 and 5711] {HED Project No. 9-1833 and 9-2027}

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THRU: Robert S. Quick, Section Head
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TO: Kerry Leifer, PM-45
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BACKGROUND

The Agricultural Division of the Ciba-Geigy Corporation has submitted amendments consisting of cover letters and supplementary Section D (revised analytical methods). The methods were submitted in response to deficiencies uncovered during the method tryout (see memorandum, D. Swineford ACB/BEAD on May 30, 1989). The deficiencies noted are repeated and listed in the body of this review as they appeared in the ACB report, followed by DEB's comments on the revised method.

Our conclusion and recommendation follow:

CONCLUSIONS

The petitioner has satisfactorily addressed the concerns noted in the ACB report, namely that the same solvents are used for the standard and sample injection, preparation of standards is better explained, additional cleanup has been incorporated into the method, not as an optional step, and problems relating to a multiple peaked standard are resolved. The method (AG-536C) is suitable to gather residue data. DEB reiterates that the only remaining analytical method deficiency is for residue method (AG-536C) to undergo a successful PMV. DEB can not recommend for a tolerance without a successful PMV. Thus, the deficiency noted in our review of April 3, 1989 (see memo by FDG) continues unresolved and remains outstanding.

RECOMMENDATION

DEB is submitting method AG-536C to ACB/BEAD for a new petition method validation (PMV) on corn forage at 0.01 ppm and 0.02 ppm.

However, DEB can not, at this time, recommend for the proposed tolerance of CGA-154281 on all crops with a tolerance for metolachlor for the reasons cited above in our conclusion.

Detailed Considerations

Residue Analytical Method Deficiencies as Stated by ACB.

1. The submitted method for the quantitative analysis of CGA-154281 indicated that for the method to be successful it is imperative for the gas chromatographic (G.C.) standard used for quantitation be made with 20% dodecane in iso-octane to enhance the GC response of CGA-154281 as compared with the sample extract contained in 100% iso-octane (Method - Section II.H.5. and No. 4 and under comments for: Laboratory Report No. 1 - Job #88-196). This is not a scientifically valid approach. Why not dilute the sample by some arbitrary amount to show good recovery data? Triple injections of the two standards analyzed in duplicate at the 1.0 ng level showed a 268% greater response for CGA-154281 made with 20% dodecane in iso-octane than the same amount of standard in 100% iso-octane.

2. G.C. chromatograms submitted with the method represent a very narrow window of approximately 2 minutes of retention time. This does not allow for a complete evaluation of the G.C. analytical data. The G.C. parameters show that the chromatograms are attenuated for the majority of the chromatographic run to show a level baseline and the attenuation is changed just prior to the single peak suggested for CA-154281.

Our G.C. analyses of CGA-154281 Lot #ACK1, purity 99.4% obtained from the Environmental Protection Agency Pesticide Repository a Research Triangle Park, NC and evaluated at the same GC conditions as the submitted method except for the attenuation revealed several major chromatographic peaks representing approximately 10,20 and 70% of the total peak area for the chromatogram for a 40 ng injection of the standard.

The method does not indicate the presence of multiple peaks in the CGA 154281 standard. This could result in serious error if the wrong peak is identified in the retention window.

3. Analysis of 25g aliquot of corn forage control and corn forage spiked at 0.01 and 0.02 ppm by the submitted method did not allow for the separation and accurate quantitation of CGA-154281 from the background of the corn forage matrix. The problem of high levels of interference for the analysis of corn fodder is also mentioned in comments number 6 of Ciba-Geigy Job #88-196 (Report #1).

Petitioner's Responses (See MRID No. 411774-01 and 412108-02)

As a result of the June 27, 1989 EPA/Ciba-Geigy meeting, the petitioner decided to submit a revised method (the July 7, 1989 amendment), and not to use FDA's multiresidue methods to enforce the suggested tolerance. The title of the method is "Analytical Method of the Determination of CGA-154281 in Crops by Capillary Gas Chromatography" by R. E. M. Wurz dated July 7, 1989 and coded AG-536B. As a result of telecons (F. D. Griffith EPA -L. Ballantine Ciba-Geigy on August 17, 1989) additional problems with the analytical standard preparation were uncovered, thus the amendment of August 21, 1989 was submitted. The title of this revised method is "Analytical Method for the Determination of CGA-154281 in Crops by Capillary Gas Chromatograph" by R. E. M. Wurz dated August 18, 1989 and coded AG-536C

DEB Comments

The revised method AG-536B supersedes method AG-536A (see review of September 28, 1988 for comments) and is in essence an expanded, more detailed method. Changes that the petitioner has made are in the cleanup step. Now the cleanup is through two florisil Sep Pak®s connected in tandem with an additional 15 ml elution of MTBE/hexane (3/7) to recover CGA-154281. The tandem Sep Pak®s are now part of the procedure, not an optional step. After the solvent is taken to dryness on a rotary evaporator it is made to volume 0.5 ml with dodecane/isooctane (2/8). Both standard and samples are injected into the GC in dodecane-isooctane (2/8). Minor adjustments were made in the run temperature program.

Calculations are based on peak heights using a standard curve prepared from standards in the range of 0.1 ng to 2 ng. The correlation coefficient is 0.9988 and the slope is 24.6 peak heights/ng.

Recovery/validation data for CGA-154281 were presented from corn forage fortified at levels from 0.01 ppm to 0.05 ppm. Recoveries at 0.01 ppm level (n=4) ranged from 64% to 101% and at 0.02 ppm level (n=4) ranged from 68% to 89%. The petitioner has presented adequate validation data for CGA-154281 in corn forage at the proposed tolerance level.

The petitioner also presented adequate supporting chromatographic data for a standard curve, a control and three spike samples. The four standards show no UARs from retention times of 6 through 11 minutes. Likewise on the control sample and the three spikes DEB notes there are no UAR's that interfere with CGA-154281 determination. At this point DEB can not determine a cause for ACB's standard multiple peak response. A new standard of CGA-154281 has been supplied to ACB and it will have to be compared to the existing standard at RTP. DEB also invites comments from the petitioner on changing the injection liner more frequently then once every 10 to 20 injections. DEB suggests a standard-sample injection approach to routine analyses and change the injection liner at the first indication of multi-peaks, or 10 injection which ever comes first.

Method AG-536C supersedes AG-536B. It is a more detailed version of the original method. The only difference between methods AG-536B and AG-536C involves preparation and handling of the analytical standard. Solutions of the standard once prepared in dodecane/isooctane (2/8) are stored in amber round bottles and refrigerated when not use. The petitioner informs us the standards are stable at least 2 months when stored in amber glass and refrigerated. DEB considers this to be a valuable instruction as CGA-154281 is a light sensitive compound.

DEB concludes method AG-536C is suitable to gather residue data. Since deficiencies noted in ACB's report have been incorporated in a more detailed write up with new supporting validation data, DEB recommends for a new PMV using method AG536C.

H-7509C:DEB:Reviewer(FDG):CM#2:Rm814B:557-0826:
eb:8/31/89:edited:fdg:8/31/89.
cc:PP#7E3489,R.F.,Circu(7),Reviewer(FDG),ACB(Marlow),Repository (Thompson),ISB/PMSD(Eldredge).
RDI:Section Head:R.S.Quick:9/1/89:R.A.Loranger:9/1/89.